CLOZAPINE TREATMENT

SECTION CONTENTS

1520

CLOZAPINE TREATMENT

INTRODUCTION

General Requirement

In order to optimize the safe use of clozapine and limit the risk of potentially fatal outcomes, CONREP programs with clozapine patients shall comply with all policies and procedures specified in Section 1520. All requirements stipulated by the pharmaceutical companies and the Statewide Clozapine Patient Manager (listed in following pages) must be implemented.

Background

Description

Clozapine is the *generic* name for a unique antipsychotic drug. Clozapine is dispensed under the *brand* name Clozaril by Novartis**.** Clozaril may also be dispensed as Clozapine unless the prescribing physician states brand name only. Clozapine is available in a generic form from Zenith Goldline Pharmaceuticals. Information utilizing either name refers to the same drug.

Usage

Clozapine is particularly successful for some treatment-resistant schizophrenic patients who have been unresponsive to standard antipsychotic drug treatment. It has done so with a markedly reduced incidence of extrapyramidal reactions and has yet to be implicated in the production of tardive dyskinesia.

Toxicity

Approximately 3% of patients receiving this drug will experience leukopenia and 1% will experience agranulocytosis, which is potentially life-threatening. Due to this potential risk of toxicity, Novartis has stipulated a number of conditions that govern the dispensing of this drug. These conditions will be described later in this section.

Cost and Additional Procedures

There is a significant cost associated with the distribution of this drug which limit its use. In addition to the high cost of the drug itself, there are specific procedures for prescribing physicians, dispensing pharmacies and the patient to follow, including regular blood tests.

1520

CLOZAPINE TREATMENT

INTRODUCTION

Purposes of Policy

The policy regarding the use of clozapine for CONREP patients has been developed to:

* Provide programs with basic information regarding the availability and conditions associated with the distribution of this drug;

* Detail the procedures and system established to enable the drug to be administered to CONREP patients for whom it is most likely to be beneficial in a manner which minimizes risk from potential side effects;

* Establish the necessary coordination of treatment and discharge planning between state hospitals and CONREP programs in order to prevent interruptions in clozapine treatment for patients who are discharged from state hospitals while receiving the drug; and

* Enable CONREP programs to provide this medication and its associated requirements in the most effective manner.

Medi-Cal Coverage

Clozapine is available through Fee-for-Service Medi-Cal. A Treatment Authorization Request (TAR) is no longer necessary. Medi-Cal will cover the costs of the medication and laboratory work. CONREP programs should encourage eligible patients to utilize this Medi-Cal benefit.

CLOZAPINE TREATMENT

CRITERIA FOR USE

Current Patients

If a patient is under going clozapine treatment at the time of discharge from a state hospital, then it can be assumed that he or she meets the criteria for administration of this drug.

New Patients

If a CONREP director determines that a patient already in community placement would be appropriate for clozapine treatment, the patient must meet the clinical indicators listed below which reflect the current State Hospital Clozapine Protocol (Special Order 105.03, 1/1/2000).

Clinical Indicators

The following clinical indicators must be present:

* The patient must have an adequately documented diagnosis of schizophrenia or schizoaffective disorder according to current DSM criteria;

* Patients with other diagnosis may be eligible if they have tardive dyskinesia and require antipsychotic medications;

* Patients with treatment resistant bipolar disorder may all qualify;

* The patient must have at least one of the following conditions documented:

    1. Tardive dyskinesia when antipsychotic medications are required; and/or

    2. Treatment resistance for schizophrenic or schizoaffective patients, as defined below.

Treatment Resistance

Treatment resistance for schizophrenia and schizoaffective disorder is defined as treatment failures in two previous neuroleptics trial, each of which must be at least 6 weeks in duration, and which included at least one different atypical neuroleptic.

CRITERIA FOR USE

Treatment Resistance (cont.)

Patients unable to complete a full trial due to adverse reactions will qualify if the specific adverse reaction is documented and another neuroleptic of a different class less likely to cause that adverse reaction has been tried.

For the treatment of schizophrenia or schizo-affective disorder, an "adequate dose" of a typical/conventional antipsychotic drug needed to qualify for treatment failure is defined as a minimum of 600mg per day of chlorpromazine or its equivalent. The chlorpromazine equivalents of several typical antipsychotics are listed below.

Chlorpromazine Equivalents

Drug	Equivalence
Chlorpromazine	600
Thioridazine	600
Mesoridazine	300
Perphenazine	60
Loxapine	60
Molindone	60
Thiothixene	30
Trifluoperazine	30
Fluphenazine	12
Haloperidol	12
Risperidone	6
Olanzapine	20
Quetiapine	400

Contraindications

There are numerous specific contraindications and cautions in prescribing this drug which are described in the insert provided by Novartis, the Physician Desk Reference (PDR) and/or other recent literature. Any physician prescribing this drug is responsible for becoming knowledgeable about this material.

CONDITIONS FOR USE

Novartis and Zenith Requirements

Before either of the pharmaceutical companies (Novartis and Zenith) will authorize clozapine for individual patients, there are several conditions which must be met. These are described below and include both initial and ongoing responsibilities.

Clozapine Treatment System (CTS)

Any physician intending to prescribe clozapine and the pharmacy which will dispense it, must provide the distributing pharmaceutical company with specific information via a "compliance" form agreeing to follow the required procedures. This process establishes them as a registered Clozapine Treatment System (CTS).

Patient Registration

All patients must be registered with either the Novartis or Zenith National Registry and approval received prior to beginning treatment. Approval will be in the form of "Rechallenged Clearance Authorization Numbers" that will be assigned to patients. Zenith will have 24 hour access to the Novartis Registry Master File, so that either company will be able to cross check patients' registry files.

Changes in CTS

If there are any changes to the Clozapine Treatment System, (e.g. patient is returned to the state hospital, or a change in the prescribing M.D. or pharmacy), then re-registration with the National Registry is required.

Blood Monitoring

Weekly

Initial and weekly blood tests to monitor white blood cell (WBC) counts, that include a differential, are required for the first six months. These laboratory results are to be reviewed by both the physician and pharmacist before the drug is dispensed.

CONDITIONS FOR USE

Blood Monitoring (cont.)

Every Other Week	When there has been continuous clozapine therapy and no abnormal WBC counts for six months, a clinical decision may be made by the treating physician for every-other-week blood testing. Acceptable WBC counts consist of a WBC greater than or equal to 3,000/mm^3 and an absolute neutrophil count (ANC) greater than or equal to 1,5000/mm3. Physician knowledge of the patient for these 6 months is imperative. The information from the blood draws are to be provided to the Novartis National Registry each time a patient's blood is tested.
Upon Discontinuance of Drug	Blood monitoring must also be performed for a minimum of four weeks after discontinuing the medication.
Other Tests	In addition to the blood test indicated above, the following tests are recommended, to be ordered at the physician's discretion: * Full liver function panel every 6 months; and * A KUB (abdominal plate X-ray) quarterly.
Drug Dispensing	Prescriptions for Clozapine can only be filled at a pharmacy registered as part of a Clozapine Treatment System. Patients receive no more than a weekly supply of medication at each dispensing, if they are having weekly blood tests. Pharmacists may dispense a two week supply of clozapine if the physician has authorized the blood draws be performed on a biweekly basis. Pharmacists are allowed to provide one or two week supply of the drug only after verification of an appropriate WBC count in the patient's blood test. If there is no blood test result or an unacceptable WBC count, no drug is dispensed.

COORDINATION OF STATE HOSPITAL DISCHARGE

State Hospital Responsibilities

Department Policies	All of the state hospital responsibilities regarding clozapine described in this section have been issued as policies in Long Term Care Services, Special Orders No. 109, Procedures for Transitioning Patients Receiving Clozapine Treatment (4/3/95) and No. 105.03, Psychotropic Medication Guidelines and Clozapine Protocol (1/1/2000).
Notification of Clozapine Treatment	State hospitals are to provide CONREP programs with the current listing of all CONREP patients who are receiving clozapine in the state hospitals. The transfer of this information shall occur on a quarterly basis, or sooner if indicated. CONREP programs will be notified whenever clozapine treatment has been initiated or discontinued for any specific patient.
Coordinated Discharge Planning	State hospital staff are responsible for coordinating discharge planning with CONREP liaison staff. CONREP will be notified and given opportunity to participate in the final 90 day treatment planning conference prior to discharge. The following information will be provided to CONREP programs for all patients receiving clozapine treatment: * Assistance in ascertaining the patient's Medi-Cal eligibility status; * Each patient's progress and response to the medication (Form **MH 5765 Clozapine Data Report**); and * Anticipated date of discharge. Enrollment in another Clozapine Treatment System must be in place prior to discharge to the community.

COORDINATION OF STATE HOSPITAL DISCHARGE

State Hospital Responsibilities (cont.)

Trust Office Notification	State hospital staff will notify the Trust Office within 90 days prior to the patient's discharge in order to establish Medi-Cal eligibility at the time of discharge.
Clozapine Discharge Information	On the day of discharge or earlier if possible, the state hospitals will transmit Patient Discharge Information to CONREP programs (Form MH 5765) via FAX or overnight mail. This information should contain the following: * Discharge date or anticipated discharge date; * Last WBC results and date drawn; * Current dose of clozapine; * Quantity and number of days supply of clozapine to be dispensed as take-home medication; * Name and dosage of at least two other antipsychotic medications that have been treatment failures, reasons for failure and the duration of drug trials; and * Other medications the patient is currently taking.
Discharge Day	Discharge will occur early in the week, soon after the last blood count has been drawn to expedite the transfer of these functions to the community by the following week.

COORDINATION OF STATE HOSPITAL DISCHARGE

CONREP Responsibilities

Contact With Hospital Trust Office	Upon notification that a patient has been started on clozapine, CONREP liaison staff need to establish contact with the Trust Office in the state hospital in order to assist in their patient's Medi-Cal eligibility determination process.
Referral to Clozapine Treatment System	In order to maintain continuity of drug services for state hospital patients currently receiving clozapine, the CONREP program should refer the patient to the appropriate local or statewide CONREP Clozapine Treatment System prior to or immediately at the point of discharge to the community (see following pages for details).
Release of Information	Because information must regularly be sent to Novartis, patient consent for the release of information must be obtained. This release of information consent is in addition to the usual informed consent regarding medication. Programs may use form **MH 5671, Authorization for Release of Patient Information** or a comparable local program form.
Terms & Conditions of Outpatient Treatment	Procedures and requirements for clozapine treatment services are to be incorporated into each patient's Terms and Conditions of Outpatient Treatment.

CLOZAPINE TREATMENT

CONREP CLOZAPINE TREATMENT SYSTEMS (CTS)

CTS Services

The variety of services required in order to maintain a patient on clozapine have been termed a Clozapine Treatment System (CTS). A CTS should incorporate the following services:

* Patient registration in the appropriate National Registry;
* Arrangement and coordination of pharmacy and laboratory services;
* Patient compliance monitoring;
* Quality assurance monitoring;
* Reports to the appropriate national registry and prescribing physician;
* Notification to physician, pharmacy and case manager if any problems develop with compliance or lab results; and
* Coordination of services during vacation and travel away from home area.

Prescribing Physician Responsibilities

All clozapine prescriptions for CONREP patients must be prescribed by the CONREP staff (or county CTS) physician. The physician is also responsible for reviewing weekly lab results and coordinating with the pharmacy regarding weekly dispensing of the medication. The physician is also responsible for notifying the primary therapist and the appropriate CTS manager whenever there is any change in any of the patient's medications.

CONREP CLOZAPINE TREATMENT SYSTEMS (CTS)

CONREP Options

Local CTS	Where available, all CONREP programs (both county and private contractors) are encouraged to utilize the county mental health program for Medi-Cal enrollment, provision of medication, lab work and all other aspects of a CTS for both Medi-Cal and non-Medi-Cal patients.
Statewide CONREP CTS	The State Department of Mental Health has established a statewide CTS for those CONREP programs which are unable to obtain these services through county mental health programs. The statewide CONREP CTS is available to provide all non-physician clozapine related services including the provision of medication and all other aspects of CTS for Medi-Cal and non-Medi-Cal patients.
DMH Approval	If a CONREP program is unable to utilize the CTS services available within its local mental health system, approval for using the statewide CTS must be received in advance from the program's DMH CONREP Operations liaison. Such a choice must be based on compelling reasons related to fiscal factors and/or program effectiveness.

Statewide CONREP CTS Services

Statewide CTS Manager	The State has contracted with Peter B. Perrin, R.Ph., FASCP to be the statewide CONREP CTS manager. Peter Perrin, R.Ph. FASCP Independent Consultant Pharmacist Services, Inc. 3051 Fujita Street Torrance, CA 90505 Phone:(310) 326-5656 FAX: (310) 326-5654

CONREP CLOZAPINE TREATMENT SYSTEMS (CTS)

Statewide CONREP CTS Services (cont.)

Specific Services	The statewide CONREP CTS manager will coordinate all clozapine related services for referred patients. All prescription, pharmacy and lab information will be forwarded to the contractor. In addition to all CTS services listed earlier in this section, the statewide CONREP CTS manager will issue clozapine patient identification cards and provide clinical pharmacist consultation.
Hospital Discharge Referral Process	In order to begin coordinating discharge plans with the CTS Statewide Manager, a written referral utilizing DMH form **MH 7007, Clozapine Referral Information Sheet** should be initiated by CONREP within 30 days of an anticipated admission date for any clozapine patient requiring these services. At the same time, the discharging state hospital should also forward DMH form **MH 5765, Clozapine Data Report**. Both referral forms should be forwarded to the statewide CONREP CTS manager (see address on previous page).
Initial Referral Information	The written referral prior to hospital discharge should contain the following information: * Patient name; * State hospital or location of patient; * Expected date of discharge to community; * Location of planned residence and phone number, if known; and * Identification and phone number of primary therapist.

CONREP CLOZAPINE TREATMENT SYSTEMS (CTS)

Statewide CONREP CTS Services (cont.)

Notification of Discharge or Transfer from CONREP

CONREP programs are to notify the statewide CTS manager of the pending discharge from CONREP or transfer to another CONREP program of any patient receiving clozapine whom the manager has been monitoring. Within 30 days prior to the anticipated date of discharge, forward the following information to the statewide CTS manager via FAX:

* Patient's name;
* Expected date of discharge;
* Name and phone number of CONREP contact person coordinating the discharge;
* Name, contact person and phone number of new program, if clozapine treatment is to continue.

Also, FAX the final date of discharge and any relevant discharge information. The CTS manager will coordinate the transition of clozapine monitoring functions to the new program.

Clozapine Services Plan

Each CONREP program must file a plan with the Forensic Services, CONREP Operations Office describing how clozapine services will be provided to its patients. The plan should include identification of:

* Which CTS (local or statewide CONREP) will be utilized;
* The CTS manager;
* Who will perform the duties and functions identified under CTS Services (see page 1520.10); and
* The jail contact person with the assigned responsibilities.

PROGRAM CONCERNS

Patient Support

The patient's primary therapist should incorporate the requirements for weekly lab work and pharmacy visits to the patient's individual treatment plan and help coordinate and support the patient's ability to make these weekly appointments.

Observation

All CONREP staff involved with the patient should monitor the patient's behavior, progress and response to the medication. Any concerns are to be reported to the physician on staff.

Patient Compliance

All CONREP staff involved with the patient shall report any information concerning the patient's non-compliance with clozapine requirements (e.g. failure to take medication and/or failure to appear for laboratory work) to the primary therapist, who is then responsible for the contacting the CTS manager.

Vacation and Travel

In the event that a clozapine patient is traveling or on vacation, the CONREP program staff physician or primary therapist must notify their CTS manager. The CTS manager will then make arrangements with a registered Clozapine Treatment System in the travel destination and provide the patient with specific instructions on procedures to maintain necessary lab work and pharmacy services.

A current list of all registered Clozapine Treatment Systems is available through the Novartis National Registry: 1-800-448-5938.

The Statewide CTS Manager, Peter Perrin, R.Ph, FASCP of ICPS can assist programs with vacation, travel and relocation concerns related to clozapine. (Please see earlier pages.)

PROGRAM CONCERNS

Notification of Status Change

If a CONREP patient receiving clozapine has been rehospitalized, jailed or placed in any institution, it is the CONREP program's responsibility to promptly notify the CTS manager. For rehospitalizations, it is important to also indicate a timeline for the patient's return to the community.

Jailed Patients

CTS Notice

When a CONREP patient receiving clozapine has been jailed, the name of the appropriate contact within the jail system must also be identified for the CTS manager. The jail contact will be responsible for providing the CTS manager access to the patient and/or the administration of the medication.

If the patient is under the management of the statewide CONREP CTS manager, the Community Program Director or designee shall notify the jail contact. This notification will identify the CONREP statewide clozapine patient manager and indicate his need to have access to the patient and all relevant information in order to assure that the patient continues to receive the medication and all lab work.

Problems

If any problems arise concerning access to the patient in jail, the provision of medication or clozapine related treatment services, the CTS manager will notify the Community Program Director. It is the responsibility of the Community Program Director or designee to attempt to resolve those problems in concert with jail authorities so that clozapine treatment can be maintained.

Non-CONREP Patients

CONREP is only responsible for providing this liaison function for patients already admitted to its program. *CONREP is not responsible for those state hospital patients on court leave status.*

CLOZAPINE TREATMENT

MEDI-CAL PROCEDURES

Eligibility

Determination of eligibility and enrollment in the Medi-Cal program must be made by the state hospital trust office prior to seeking authorization for Medi-Cal to fund clozapine and its related laboratory services. (See prior sub-section on Coordination of State Hospital Discharge.)

Medi-Cal Guidelines for Clozapine

Medi-Cal guidelines require the following:

* Evidence of a diagnosis of severe schizophrenia or schizoaffective disorder;

* Demonstrated history of treatment failure on two conventional neuroleptics (antipsychotic drugs) in separate trials. A neuroleptic trial is defined as at least four continuous weeks of treatment at an adequate dosage; and

* Patients with severe tardive dyskinesia may qualify for approval without history of neuroleptic treatment failure or the foregoing multiple neuroleptic trials.

Medi-Cal Drug Unit Field Offices

Programs may contact the appropriate Medi-Cal Drug Unit field office as follows for any Medi-Cal related concerns regarding clozapine treatment:

* Southern California Counties:
(Imperial, Inyo, Kern, Los Angeles, Mono, Orange, Riverside, San Bernardino, San Diego, and Ventura.)

Contact the Los Angeles Office:
213-897-1238.

* Northern California Counties:
(All other counties)

Contact the Stockton Office: 209-942-6030.